

REMARKS

Entry of the Amendment is respectfully requested. Applicants submit the Amendment places the application in condition for allowance and raises no issues not previously considered by the Examiner.

Claims 36, 37, 40, 45, 47, and 50 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Claims 32, 38, 39, 43, 44, 46, 48, 49, and 53 have been amended to further clarify the invention. Claims 54 to 71 are newly presented. Applicants submit the amended claims and newly presented claims are supported throughout the specification, including at page 14, line 14 to page 15, line 3, at page 16, lines 18-30, at page 33, lines 17-23, at page 83, lines 11-19, and at page 84, lines 24 to page 85, lines 4, and present no issues of new matter.

After entry of the Amendment, claims 32, 35, 38, 39, 41-44, 46, 48, 49, and 51-71 are pending.

Obviousness

The Examiner rejected claims 32, 36, 38-45, and 47-49 under 35 U.S.C. § 103(a) as being unpatentable over Lai et al., 2000, *Genome Res.*, 10:703-713. Applicants respectfully traverse this rejection.

The Examiner bears the initial burden of factually supporting any prima facie conclusion of obviousness. MPEP § 2142. Three criteria must be met by the Examiner to establish a prima facie case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner has failed in the least to establish that Lai et al. teach or suggest all the limitations of Applicants' claims.

Applicants' claims, as amended, are directed to methods of detecting a variant CGI-69 polynucleotide. Lai et al. do not teach or suggest variant forms of CGI-69 such as, for example, a polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 98%

sequence identity to SEQ ID NO:3. Lai et al. do not teach or suggest a probe that hybridizes to a polynucleotide comprising a nucleic acid sequence corresponding to nucleotides 265 to 288 of SEQ ID NO:1. Lai et al. do not teach or suggest a probe that hybridizes to a polynucleotide comprising a nucleic acid sequence that encodes an amino acid sequence corresponding to amino acid residues 65 to 72 of SEQ ID NO:3. Lai et al. therefore do not teach or suggest all the elements of Applicants claims.

Moreover, one of skill in the art would not be motivated by reading Lai et al, to modify the sequence. Lai et al is directed to identifying genes that are homologous to those of *C. elegans*. The identification is done by searching databases. There is no disclosure or suggestion of modifying such genes or even why modification would be desirable. The Lai et al reference provides no teaching or suggestion that genes encoding a polypeptide relating to SEQ ID NO:3 are expressed and/or differentially expressed in tissues.

In view of the foregoing, Applicants submit the Examiner has failed to establish a prima facie case of obviousness. The Examiner has failed in the least to establish that Lai et al. teach or suggest all the limitations of Applicants' claims and to establish a motivation for modification of the sequence. Applicants respectfully request withdrawal of the obviousness rejection.

Enablement

The Examiner rejected claims 32, 35, 36, and 38-53 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner alleges the specification does not enable any person skilled in the art to use the invention of the claims. Applicants respectfully traverse this rejection.

The legal standard for enablement under 35 U.S.C. § 112 requires that "[...] a patent specification must disclose sufficient information to enable **those skilled in the art** to make the claimed invention." *Hormone Research Foundation, Inc. v. Genentech*, 15 USPQ2d 1039, 1047 (Fed. Cir. 1990). It is a well accepted premise that §112¶1 requires only that a patent specification describe to one of ordinary skill in the art how to make and use the claimed invention without **undue** experimentation. The enablement requirement is met if the description enables any mode of making and using the claimed invention. *Engel Ind. v. Lockformer Co.*, 946 F.2d 1528 (Fed. Cir. 1991). If any use is enabled when multiple uses are disclosed, the

application is enabling for the claimed invention. MPEP § 2164.01(c).

Applicants' claims are directed to methods for identifying variant CGI-69 polynucleotides from a biological sample. Applicants submit the specification provides considerable direction and guidance on how to practice the claimed invention, including working examples. Applicants provided several examples of variant CGI-69 polynucleotides and the nucleic acid sequences of the probes used to identify the polynucleotides. The claimed methods are useful for identifying cells that express CGI-69 polypeptides and assessing, measuring or quantitating cellular respiration in these cells, as taught for example in Example 3. In view of the disclosure, one skilled in the art would have been able to use the claimed methods to identify variant CGI-69 polynucleotides from a biological sample without undue experimentation. Applicants submit this use is sufficient to meet the enablement requirement.

The Examiner asserts that there is no evidence of correlation of CGI-69 and variants to metabolic disorders or other biological function, and given that lack of correlation there is no utility in one of skill in the art practicing the claimed invention. Applicants respectfully disagree.

Applicants demonstrated that human CGI-69 has 86% amino acid sequence identity with murine CGI-69. Murine CGI-69 was found to be upregulated 2 fold BAT in cold-challenged mice, indicating a role in BAT thermogenesis. Analysis of the human CGI-69 protein structure indicated the presence of 4 mitochondrial carrier domains, 6 potential transmembrane spanning domains, a likely mitochondrial localization, and 3 regions with reasonable homologies to putative mitochondrial energy transfer signature sequence in known UCP homologs. Mitochondrial localization was confirmed using labeled CGI-69. Based on the significant amino acid sequence identity and structural similarities to mouse CGI-69, Applicants submit one skilled in the art would have expected CGI-69 to be a mitochondrial carrier protein.

The Examiner asserts Adams teaches that studies correlating expression of UCP1 homologs with metabolic status did not yield compelling evidence to confirm an important contribution of any homologs' activity toward driving metabolic rate in vivo. Applicants do not agree with the Examiner's characterization and further submit that the Adams reference must be considered as a whole. When the Adams reference is considered as a whole, Adams teaches that a number of findings associated with the UCP homologs are consistent with an uncoupling

function. Numerous positive correlations are outlined in Adams suggesting UCP homologs have uncoupling activity. For example, similar to UCP1, which drives thermogenesis in BAT, UCP2, UCP3, UCP4, and UCP5 elicit a drop in Δp , which is consistent with an uncoupling activity. UCP2 expression in BAT was found to rise in response to cold concurrently with UCP1 expression and BAT thermogenesis (Adams at page 712). Relatively abundant expression of UCP3 in skeletal muscle and rodent BAT appeared consistent with the characterization of UCP3 as a thermogenic protein. (Adams at 712). UCP2 and UCP3 genes are located near a region linked to metabolic rate (Adams at 712). After a 3-week high fat dietary regimen, liver UCP5 expression in obesity resistance mice was significantly elevated compared with obesity prone mice (Adams at 713). Cold exposure in mice also sparked induction of UCP5 mRNA in the liver and brain potentially signally increased thermogenesis (Adams at 713). In view of the positive correlations set forth in Adams, Applicants submit one of skill in the art would have predicted that UCP homologs influence metabolic rate.

Based on the foregoing, Applicants submit one of skill in the art would have been able to use the claimed methods without undue experimentation. The level of skill in the art is high and the specification provides considerable direction and guidance on how to practice the claimed invention, including working examples. Accordingly, withdrawal of the enablement rejection is respectfully requested.

Written Description

The Examiner rejected claims 32, 35, 36, and 38-53 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges the specification provides insufficient written description to support the genus encompassed by the claims. Claims 35, 36, 45, 46, 47, and 50 have been canceled without prejudice or disclaimer. Applicants traverse with respect to the other claims.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish

it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added).

Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed. Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Applicants' claims are directed to identifying a polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 98% sequence identity to SEQ ID NO:3. Applicants submit the specification as filed provides written description for the claimed invention.

Applicants submit the specification adequately describes polynucleotides encoding such a polypeptide. See, for example:

Table 1 at page 10

Table 3 at page 14

Page 21, lines 9-14

Ordinarily, an CGI-69 variant polynucleotide with have at least about 80% nucleic acid sequence identity, more preferably at least about 82%, 83%, 84%, 85% 96%, 87%, 88%, 89%. 90% 91%, 92%, 93%, 95%, 95%, 96%, 97%, 98% nucleic acid sequence identity with the nucleic acid sequence encoding a full-length native CGI-69.

Page 33, lines 17-23

An CGI-69 polypeptide variant will have at least about 80% amino acid sequence identity, more preferably at least about 82%, 83%, 84%, 85% 96%, 87%, 88%, 89%. 90% 91%, 92%, 93%, 95%, 95%, 96%, 97%, 98% amino acid sequence identity and most preferably at least about 99% amino acid sequence identity with a full-length native sequence CGI-69 polypeptide sequence.

The level of skill in the art is high. Therefore, one of skill in the art would have envisioned the scope of the probes and primers within the scope of the claims based on the disclosure of SEQ ID NOs:1 and 3. The specification, for example, teaches a number of probes and primers are useful for identifying human CGI-69, human CGI_L-69, or mouse CGI-69 (Specification at page 84, line 19 to page 85, line 3). Moreover, comparison of the amino acid and nucleic acid sequences of CGI-69 and CGI_L-69 revealed that CGI_L-69 may be distinguished from CGI-69 by an amino acid sequence corresponding to amino acid residues 65 to 72 of SEQ ID NO:3 or a nucleic acid sequence corresponding to nucleotides 265 to 288 of SEQ ID NO:1.

Based on the foregoing, Applicants submit one of skill in the art would have envisioned the claimed genus of polynucleotides. Withdrawal of the written description rejection is respectfully requested.

Indefiniteness

The Examiner rejected claims 32, 35, 36, and 38-53 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants submit this rejection has been obviated by the amendment. Withdrawal of this rejection is respectfully requested.

Appl. No. 09/888,358

Amdt. dated September 7, 2004

Reply to Final Office Action of November 10, 2003 and Notice of Appeal dated May 7, 2004

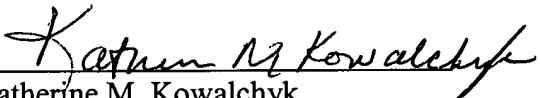
Conclusion

In light of the forgoing Amendment and Remarks, Applicants' assert the claims are in condition for allowance. Early notice of allowable claims is requested. The Examiner is invited to telephone the undersigned attorney for clarification of any of these Remarks or Amendments, or to otherwise speed prosecution of this case.

Respectfully submitted,

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